IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Kenneth K. Sokoll	Confirmation No:	1691
Serial No.:	10/076,674	Examiner:	Emily M. Le
Filing Issue Date:	February 14, 2002	Group Art Unit:	1648
Title:	STABILIZED SYNTHETIC IMMUNOGEN DELIVERY SYSTEM		

Mail Stop Appeal Brief
Commissioner of Patents
P.O. Box 1450
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Sir:

APPEAL BRIEF

Applicant submits this Appeal Brief in support of its Notice of Appeal filed on December 19, 2007. Also enclosed is a Petition to Extend the time for filing the Appeal Brief for one month. The Commissioner is authorized to charge the requisite fee under §41.20(b)(2) in the amount of $510.00, and any additional fees necessitated by this Brief to deposit account no. 13-4500 (Order No. 1151-4172).

Applicant respectfully requests that this Brief be fully considered by the Board and that the Examiner's rejection of the claims be reversed for the reasons stated herein.

I. THE REAL PARTY IN INTEREST

The real party in interest for this application is the assignee, United Biomedical, Inc. The assignment was recorded on February 14, 2002 at Reel/Frame: 012609/0616.

II. RELATED APPEALS AND INTERFERENCES

There are no other appeals or interferences known to the Appellant, the Appellant's legal representative, that will directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

III. THE STATUS OF THE CLAIMS

The claims now pending are Claims 1, 4-10, 12-13, and 18-19. Claims 2-3, and 11 are cancelled and claims 14-17, 20-75 are withdrawn subject to a restriction requirement and the subject matter in presented in a related application, Serial No. 10/355,161.

IV. STATUS OF AMENDMENT

A response to the final rejection was filed on December 18, 2007. The Response included a request for reconsideration and supporting arguments and a declaration under 37 C.F.R. § 1.132. The Response includes an amendment of claim 1 to correct a clerical mistake. Up to the present, no Advisory Action has been received.

On January 27, 2008 and January 29, 2008 by telephone inquiring into the status of the advisory action. On January 29, 2008, the Examiner indicated that she expects to issue the advisory action within the week. Up to the present, the advisory action has not been received. A check into the PAIR system indicates the a view via the private PAIR is not available on February 10, 2008.

The present paper is based on the assumption that the minor clerical correction in claim 1 to add the word "an" before "anionic CpG oligonucleotide" is acceptable and has been entered.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The claims on appeal are drawn to a stabilized peptide immunostimulatory complex. The immunostimulatory complex is in the form of microparticles wherein a peptide immunogen is stabilized. The complex consists of a synthetic peptide immunogen, a combination of a B-cell epitope or a CTL epitope with a T helper cell epitope, in combination with a CpG oligonucleotide. The peptide immunogen is synthesized in such a manner that the B-

cell epitope or CTL epitope and T helper cell epitope combination has a net positive charge at a pH in the range of 5.0 to 8.0. The CpG oligonucleotide is a single stranded DNA comprising 8 to 64 nucleotides with a repeat of cytosine-guanidine motif. The CpG oligonucleotide is rendered anionic at a pH in the range of 5.0 to 8.0 by the presence of a phosphorothioate or a thioacetoamido glycopolymer at the 5' end.

The positively charged peptide immunogen forms a complex with the negatively charged CpG oliogonucleotide in the form of microparticles, which has been found to be surprisingly stable.

The stabilized peptide immunostimulatory complex is suitable for formulation into a vaccine composition and has the further advantages of providing adjuvantation and upregulation of immune responses in vivo.

Heretofore, vaccines formulated from a synthetic peptide immunogen suffer from instability and are easily degraded. Previous methods of stabilizing a peptide immunogen employ methods involving the embedding the peptide immunogen in an liposome, a water-in-oil emulsion or water in oil in water double emulsion. Such previous processes are cumbersome and difficult to scale up for commercial production.

The claimed invention has the advantage of being simple in that a peptide immunogen, synthesized form a B-cell epitope or a CTL epitope conjugated a T helper cell epitope is such that it is positively charged or rendered positively charge at a pH in the range of 5.0 to 8.0. The charge of the peptide immunogen is determined by selecting one having a presence of lysine, arginine or histidine in its amino acid sequence, each of which is assigned a positive charge. If the peptide immunogen is itself neutral without charge, then a lysine, an arginine or histidine is added to the selected peptide immunogen to render it positively charged.

The positively charged peptide immunogen is combined with a CpG oligonucleotide that is rendered anionic by the presence of a phosphorothioate or a thioacetanido glycopolymer at the 5'end or selected by the presence of a phosphorothioate or a thioacetoamido glycopolymer on the CpG oligonuceotide or the conversion of any labile phosphodiester group on the CpG oliogonucleotde to a phospohorothioate group. The combination of the cationic peptide immunogen with the anionic CpG oligonucleotide forms a complex in the form of microparticles and is stable. Moreover, the stabilized complex immunogen is self adjuvanting. There is no need to add prior known adjuvants, such as Alum salts, which had led to immunogen tolerance or undesired side reactions, swelling and redness at the site of injection.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

1. Whether the pending claims 1, 5, 7-9, 12-13 and 18-19 are unpatentable, i.e., obvious, under 35 U.S.C. 103(a) over Krieg et al, WO 01/22972, in view of Ladd et al., WO 94/25060.

2. Whether pending claims 1, 4 and 6 are unpatentable, i.e., obvious, under 35 U.S.C. 103(a) over Krieg et al. in view of Ladd et al. the same references indicated above.

VII. GROUPING OF CLAIMS

The pending claims were separately grouped two groups by the Examiner 1, 5, 7-9, 12-13 and 18-19 and claims 1, 4 and 6 in the final office action.

It is not entirely clear the basis of the separation of the claims into two groups for examination since Claim 1 is the only independent claim and defines a stabilized peptide immunogen complex of a positively charged Bell-cell epitope or a CTL epitope and T helper cell epitope combination with a negatively charged CPG oligonucleotide all at pH in the range of 5.0 to 8.0.

Claim 4 defines a stabilized peptide immunogen wherein the peptide immunogen is a mixture of peptide immunnogens.

Claims 5 and 6 depend on claims 1 or claim 4 respectively and define a peptide immunogen wherein the peptide immunogen has a positive charge of at least +2.

Claim 7 depends on claims 5 or 6 and defines a stabilized peptide immunogen wherein the CpG oligonucleotide has a net negative charge of at least -2.

Claim 8 depends on claim 1 and defines a stabilized peptide immunogen wherein the CpG oligonucleotide is a single stranded DNA with 18-48 nucleotide bases and repeats of the CpG motif in the range of 3 to 8.

Claims 9-10 and 12-13 depends on claim 1 and further specifies the CpG oligonucleotide formulae.

Claims 18 depends on claim 12, wherein the peptide immunogen is defined to be s synthetic peptide conjugated to a T helper cell epitope.

Claim 19 specifies the synthetic peptide as being SEQ ID NO:7, 8 or 9 or a mixture thereof.

Claim 20 specifies the synthetic petide as being a mixture of SEQ ID NO:7, 8 and 9.

VIII. ARGUMENT

A. Claims 1, 5, 7-9, 12-13 and 18-19 Are Not Obvious in view of the Combination of Krieg et al., WO 01/22972, and Ladd et al., WO 94/25060

Claims 1, 5, 7-9, 12-13 and 18-19 were rejected as being unpatentable under 35 U.S.C. § 103(a) over Krieg et al, WO 01/22972 in view of Ladd et al. WO 94/25060.

The standard for establishing whether an invention is patentable is expressly

stated:

35 U.S.C.§103(a):

> A patent may not be obtained though the invention is not identically disclosed as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was mad to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Supreme Court in Graham v. John Deere Co., 383 U.S. 1, 17 (1966):

> Under 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or non-obviousness of the subject matter is determined. …

Thus to establish a prima facie case of obviousness, the invention claimed is to be examined as a whole against the content of the prior art. It is the burden of the Examiner to prove that each and every element of the claim has been met by the disclosure, teaching or suggestion in the prior art, or the prior art as a whole when placed before the skill in the art at the time invention was made would render the claimed invention obvious. In carrying out this burden, it is impermissible to use the disclosure or teaching of the applicant. In re Sporck, 301 F.2d 686 (CCPA 1962).

The Supreme Court stated in a recent case:

> "A fact finder should be aware, of course of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning." KSR Int'l Co. v Teleflex Inc. 127 S. Ct. 1727, 1742 (2007).

i. The invention of claims 1, 5, 7-9, 12-13 and 18-19

The broadest claim is Claim 1 is directed to a stabilized immunostimulatory

microparticulate complex comprising a cationic peptide immunogen that comprises a target B cell antigen or a CTL epitope and a T helper cell epitope in combination with an anionic CpG oligonucleotide. The CpG oligonucletide is anionic or has a net negative charge at a pH in the range of 5.0 to 8.0.

The specification describes how to determine the anionic charge of the CpG oligonucleotide by examining the presence of phosphodiester or phosphorothioate groups, each of which is assigned a charge of -1. It is important to recognize that the phosphodiester in a backbone of a CpG oligonucleotide is unstable. Thus, the CpG oligonucleotide may be modified to obtain a negatively charged moiety by the addition of a phosphorothioate group or a thiooacetomido glycopolymer at the 5' end.

ii. The Prior Art

a. Krieg et al, WO 01/22972

A careful review of Krieg et al. shows that Krieg et al is directed to Pyrimidine rich, preferably thymidine rich oligodeoxynucleotides (ODN) which do not require a CpG motif. Krieg et al teaches that such pyrimidine or thymidine rich ODNs are immunostimulatory. Some of the pyrimidine or thymidine rich ODNs are CpG oligonucleotides. Krieg et al provided numerous examples of ODNs as immunostimulatory. Nowhere in the 156 pages of the specification or the 105 claims is the word "anionic" or the phrase "net negative charge" to be found.

As pointed out by the Examiner Krieg et al taught combining the pyrimidine or thymidine rich ODNs with immunotherapeutic agents for anti-cancer therapy and concedes that:

> "While it is noted that it is not readily apparent if the immunotherapeutic agents listed by Krieg et al., though not intended to be fully encompassing, includes a cationic peptide

immunogen."

The Examiner immediately concludes that there is motivation to combine the pyrimidine or thymidine rich ODNs with a peptide immunogen such as that disclosed by Ladd et al.

In the lengthy disclosure of Krieg et al. describes a variety of therapeutic agents that may be used in combination with the immunostimulatory ODNs. These are described and listed on pages 14 – 16, 62-114. The therapeutic agents include chemotherapeutic agents, vaccines, or antibody. The immunostimulatory ODN's are to be used in conjunction with the therapeutic agents. See page 14, lines 19-21.

A thorough review of the therapeutic agents that are used in conjuction with the immunostimulatory ODN's show that none are the peptide immunogens of the present invention. Krieg et al. lists chemotherapeutic agents on page 15-16. These are the known chemotherapeutic agents such as methotrexate, adriamycin, cisplatin, etc. These are proteins toxins, none of which is a peptide immunogen. Retroviral agents are disclosed on page 17. These are not peptide immunogens. Anti-bacterial agents are discuss on page 17. Again, these are not the peptide immunogens of the claims pending before the Examiner.

All of the listed therapeutic agents are stable compounds. There is no discussion or concern with their stability.

The method of administering the immunostimulatory ODNs with an anti-cancer therapeutic agent is described on page 18, lines 19-26. The immunostimulatory ODN is put into one container, and the anti-cancer therapeutic agents is put into another container. Thus, the immunostimulatory ODN is not complexed with the anti-cancer therapy agent. There is no discussion of complexing the immunostimulatory ODN with the anti-cancer agent.

Krieg et al. is not concerned with the stability of peptide immunogens in vivo or ex vivo and does not mention or recognize the need to stabilize the peptide immunogens. In fact, Krieg et al. disclosed the use of phosphodiester oligonucleotides with CpG motif as producing the maximal effect. However, the specification of the present application at page 27 [0076] states specifically that the phosphodiester bond is unstable and the phosphodiester group may be modified to a phosphorothioate group.

Moreover, no where in Krieg et al. is there a description, a teach or suggestion of negatively charged or anionic pyrimidine or thymidine rich ODNs or CpG oligonucleotide at any pH nor how to modify it if it were not anionic. More important, Krieg et al. does not disclose, teach or suggest a method of rendering a CpG oligonucleotide anionic by modifying the CpG oligonucleotide with a phosphorothioate group or a thioacetamido glycopolymer to convert it to an anionic oligonucleotide if it is not.

The Examiner points to SEQ ID NO:1 of claim 12 and states that "it is a single stranded DNA of 32 nucleic acid residues in length having 5 repeats of a cytosine-guanidine motif, and a net negative charge of -32 at a pH in the range of 5.0 to 8.0." It is nor clear how the Examiner arrived at a conclusion that SEQ ID NO:1 has a net negative charge of -32 at a pH in the range of 5.0-8.0. It appears that the Examiner has assigned a negative charge of -1 to each nucleic acid residue. It is to be noted that to a person of ordinary sill in the art, each nucleic acid is neutral with a charge of 0. Thus, even if Krieg et al. describes a CpG oligonucucleotide with the sequence of SEQ ID NO:1, there is nothing to indicate that it is anionic or negatively charges. The Examiner has attempted to apply the teachings of Applicant's description, albeit in error, to Krieg et al. to arrive at a conclusion that Krieg et al. describes anionic CpG oligonucleotides.

There is no description of a peptide immunogen in Krieg et al. nor any teaching, disclosure or suggestion in Krieg et al of the use of an anionic CpG and to form a stabilized immunogen complex with a peptide immunogen that is cationic or has a net positive charge. This, the Examiner has conceded in the final rejection on Page 3.

As stated by the Examiner, Krieg et al taught the administration of a combination of pyrimidine or thymidine rich ODNs with anti-cancer therapeutic agents, which are known to be stable. Krieg et al. taught that the pyrimidine or thymidine rich ODNs provides immune stimulation to render the cancer therapeutic agent to be more effective. However, since Krieg et al. was not concerned with peptide immunogens, there is no discussion whatsoever about making a complex of a cationic peptide immunogen with negatively charged CpG oligonucletides to stabilize the peptide immunogen.

There is no disclosure, teaching or suggestion in Krieg et al. of how to select a peptide that is cationic nor how to render the peptide cationic by modifying the peptide with the addition of lysine, arginine, or histidine at the N- or C-terminal.

In fact, Krieg et al. teaches that some ODN are immunostimulatory and some are not. It is by testing each ODN to see if they have the ability to be immunostimulatory. See page 130 of Krieg et al. According to Krieg et al, the stimulatory effects are due to the presence of TG and not those of a phosphorothioate backbone. Based on this statement, Krieg et al. teaches against the addition of phosphorothioate moiety or a thioacetomide glycopolymer to the backbone of a CpG oligonucleotide.

b. <u>Ladd et al. WO 94/25060</u>

A review of Ladd et al. shows that Ladd et al. described LHRH conjugated to a T helper cell epitope for the sterilizing an animal. It also taught that the LHRH conjugated to T

helper cell epitope may be use in the treatment of enlarged prostate or prostate cancer. There is no disclosure , teaching or suggestion of complexing the LHRH-T helper cell epitope combination with anionic CpG oligonucleotides. Thus, there is nothing in Ladd et al. about how to determine whether a CpG oligonucleotide has a negative charge nor how to modify it if is not negatively charged. There is also nothing in Ladd et al. with respect the charge of the LHRH-T helper cell combination.

There is no discussion of the instability of peptide immunogens nor any teaching or suggestion as to how to stabilize the immunogen.

c. Combination of Krieg et al. and Ladd et al.

The Examiner contends that Krieg et al. suggested combining the CpG oligonucleotides described in his patent application with existing prostate cancer immunotherapies. And, the Examiner conends that the cancer immunotherapies of Krieg et al renders it obvious to combine it with Ladd's LHRH conjugated to a T helper cell epitope.

A thorough review of Krieg et al shows that prostate cancer therapeutic compositions are listed in Table C, page 105, both of the immunotherapies described for prostate cancer are monoclonal antibodies, which are NOT peptide immunogens. In fact, a thorough review of Krieg et al, Table C shows that the immunotherapies within Krieg et al's purview are monoclonal antibodies or fragments thereof. Also see page 103 to 104. None of these remotely suggest a peptide immunogen.

As stated previously, there is no basis for the Examiner's determination that SEQ ID NO: 1 has a -32 negative charge. If it is as the Examiner contends that each nucleotide has a negative charge of -1 at pH of 5.0 to 8.0, there has to be something in the prior art cited to provide a basis for this finding. It is to be noted that the Applicant has indicated a +2 charge for

the cationic peptide is preferable. It would defy scientific principles to be able to form a stable immunogen with 16 to 32 cationic peptide to one CpG oligonucleotide.

It appears that this finding of negatively charged CpG oligonucleotides is based on applicant's discussion of how to determine if a CpG oligonucleotide is negatively charged. However, Applicant wish to point out that the specification teaches at page 16 [0037], that the negative charge of the CpG oligonucleotide is based on the presence of a phosphodiester or a phosphorothioate group and not the nucleic acids in the CpG oligonucleotide sequence itself. See page 24 [0065].

There is nothing in Krieg et al. with respect to the combination of an anionic CpG oligonucleotide with a cationic peptide comprising a B cell epitope or a CTL epitope and a T helper epitope. There is nothing in Krieg et al on how to determine if a peptide is cationic or how to render a peptide to be cationic. A review of Ladd et al. also shows that there is nothing in Ladd et al about a cationic peptide nor how to render a peptide to be cationic. Ladd et al does not disclose, teach or suggest what makes a peptide cationic nor how to make a peptide cationic by adding a lysine, arginine or histidine to its N- or C-terminal.

The use of a stabilized complex of an anionic CpG oligonucleotide with a cationic peptide is disclosed by Applicant alone and not in either of the cited references.

A review of the case law governing a finding of obviousness clearly shows that it is impressible to view prior art by reading into it the teachings provided by the Applicant. The Supreme Court stated in a recent case:

> "A fact finder should be aware, of course of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning." KSR Int'l Co. v Teleflex Inc. 127 S. Ct. 1727, 1742 (2007).

The Supreme Court's cautionary words reflect long standing case law. In In re Sporck, where the sole issue was obviousness, the Board of Appeals had concluded that the modification was an obvious adaptation over the prior art because it appeared to be a very simple modification. However, the Court of Customs and Patent Appeals held that:

> "Neither the record nor the facts judicially noticeable supplied the factual data necessary to support the legal conclusion of obviousness at the time the invention was made without substitution and hindsight appraisal of the prior art for such factual data...Once appellant's solution to the problem of making a tapered wall frusto-cone is disclosed, it is easy to see how the prior references can be modified and manipulated to produce this type of cone....However, the simplicity of new inventions is often times the very thing that is not obvious before they are made." In re Sporck, 301 F.2d 686, 689 (CCPA 1962).

The MPEP Section 2143 reflects the holding of these case decisions and states:

> "The teaching or suggesting to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure." citing In re Vaeck, 947 F.2d 488. 20 USPQ 2D 1438 (Fed. Cir. 1991)

In the present case, how to select or obtain an anionic CpG oligonucleotide is not found in the cited prior references Krieg et al or Ladd et al. The selection or obtaining a cationic peptide is not found in the cited prior references Krieg et al or Ladd et al. The formation of a stable immunogen complex using the selected or modified CpG oligonucleotide with a selected or modified peptide with a positive charge is not found in the cited prior references Krieg et al or Ladd et al. How to select or obtain an anionic CpG oligonucleotide and a cationic peptide to form a stable immunogen complex is found in Applicant's disclosure. Furthermore, it is surprising that by forming microparticles of the stabilized immunogen complex, a higher titer of antibodies is obtained. See results shown in Figs 7 and 9. Moreover, the virus neutralization

activity of the antibodies elicited is improved.

B. Rejection of Claims 1, 4 and 6

Claims 1, 4 and 6 were also rejected as being obvious in view of Krieg et al and Ladd et al for the same reasons.

Reconsideration of the rejection is requested. As stated above, it is impermissible to apply the Applicant's disclosure to the cited references to support a finding of obviousness.

For the reasons stated above, it is believed that the burden of proof of a prima facie case of obviousness relying upon the cited references, Krieg et al. and Ladd et al.

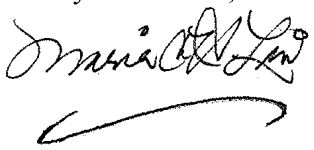
CONCLUSION

In view of the foregoing, Appellant respectfully submits that the Final Office Action has not set forth adequate grounds for the rejection of claims 1, 4-19, 12-13 and 18-19. The finding of obviousness was made applying the teachings of Applicant's specification and should be reversed. Appellant therefore requests that the Board reverse the rejections in the Final Office Action and direct the Examiner to withdraw the Office Action and allow claims 1, 4-19, 12-13 and 18-19.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be associated with the filing of this paper, or credit any overpayment, to Deposit Account No. 13-4500, Order No. 1151-4172.

Respectfully submitted,



By: _____
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Dated: February 14, 2008

IX. CLAIMS APPENDIX

1. (Amended) A stabilized immunostimulatory microparticulate complex comprising a cationic peptide immunogen wherein the peptide immunogen comprises a target B cell antigen or a CTL epitope and a T helper cell epitope and an anionic CpG oligonucleotide wherein the cationic peptide immunogen has a net positive charge at a pH in the range of 5.0 to 8.0 calculated by assigning a +1 charge for each lysine (K), arginine (R) or histidine (H), a –1 charge for each aspartic acid (D) or glutamic acid (E) and a charge of 0 for all other amino acids in the peptide immunogen and wherein the anionic CpG oligonucleotide has a net negative charge at a pH in the range of 5.0-8.0 and is a single-stranded DNA comprising 8 to 64 nucleotide bases with a repeat of a cytosine-guanidine motif and the number of repeats of the CpG motif is in the range of 1 to 10.

2-3. (Canceled)

4. The immunostimulatory microparticulate complex of claim 1, wherein the cationic peptide immunogen is a mixture of synthetic peptide immunogens.

5. The immunostimulatory microparticulate complex of claim 1, wherein the net positive charge of the cationic peptide immunogen is at least +2.

6. The immunostimulatory microparticulate complex of claim 4, wherein the average net positive charge of the mixture of synthetic peptide immunogens is at least +2.

7. The immunostimulatory microparticulate complex of claim 5 or 6, wherein the net negative charge of the anionic oligonucleotide is at least -2.

8. The immunostimulatory microparticulate complex of claim 1, wherein the CpG oligonucleotide is a single-stranded DNA molecules with 18-48 nucleotide bases and the number of repeats of CpG motif therein in the range of 3 to 8.

9. The immunostimulatory microparticulate complex of claim 1, wherein the CpG oligonucleotide has the formula: 5' X^1CGX^2 3' wherein C and G are unmethylated; and X^1 is selected from the group consisting of A (adenine), G (guanine) and T (thymine); and X^2 is C (cytosine) or T (thymine).

10. The immunostimulatory microparticulate complex of claim 1, wherein the CpG oligonucleotide has the formula: 5'$(X^3)_2CG(X^4)_2$ 3' wherein C and G are unmethylated; and X^3 is A or G, and X^4 is C or T.

11. (Cancelled)

12. The immunostimulatory microparticulate complex of claim 1, wherein CpG oligonucleotide is selected from a group consisting of 5' TCG TCG TTT TGT CGT TTT GTC GTT TTG TCG TT 3' (CpG1) SEQ ID NO: 1, a 32 base length oligomer, and 5'nTC GTC GTT TTG TCG TTT TGT CGT T 3' (CpG2) SEQ ID NO: 2, a 24 base length oligomer plus an phosphorothioate group designated as n.

13. The immunostimulatory microparticulate complex of claim 12, wherein CpG oligonucleotide is 5' TCG TCG TTT TGT CGT TTT GTC GTT TTG TCG TT 3' (CpG1) SEQ ID NO: 1.

14.-17. (Withdrawn)

18. The immunostimulatory microparticulate complex of claim 12, wherein the cationic peptide immunogen is a synthetic peptide ~~is~~ conjugated to a T helper cell epitope.

19. The immunostimulatory microparticulate complex of claim 18, wherein the cationic immunogen is selected from the group consisting of SEQ ID NO: 7, 8 and 9 and a mixture thereof.

20. -75. (withdrawn)

IX. RELATED PROCEEDINGS APPENDIX

None.